

WHAT IS CLAIMED IS:

1. A method for performing operations in small volumes with a volatile solvent, said method comprising:

5 adding a component for said operation to a liquid zone exposed to the atmosphere and containing said volatile solvent subject to evaporation, wherein said liquid zone is in contact with a replenishing medium in a capillary channel;

whereby during said operation said solvent undergoes evaporation and is replenished by said replenishing medium from said capillary channel.

10 2. A method according to Claim 1, wherein said capillary is connected to a reservoir of said replenishing medium.

15 3. A method according to Claim 1, wherein said liquid zone is in a well through a wall of said capillary channel, optionally at least a portion of the wall of said well is non-wettable, and said capillary channel is connected to two reservoirs.

20 4. A method according to Claim 1, wherein said liquid zone is expressed from the end of said capillary channel.

5. A method according to Claim 1, wherein said capillary is at least partially hydrophilic.

25 6. A method according to Claim 1, wherein the total volume of liquid in said liquid zone is not more than about 5 μ l.

7. A method according to Claim 1, wherein after said operation, at least one component in said liquid zone is transferred through a capillary channel to an electrokinesis system.

30 8. A method according to Claim 1, wherein said operation is an enzyme assay.

9. A method according to Claim 1, wherein said operation is a ligand-receptor binding assay.

10. A method according to Claim 1, wherein said operation is a reporter gene assay.

11. A method for performing a determination in a small volume, wherein said determination comprises the interaction between at least two entities, said method comprising:

adding at least a portion of said at least two entities to a liquid zone comprising a liquid exposed to the atmosphere and subject to evaporation, said liquid zone in contact with a replenishing medium in a capillary channel and having a substantially fixed meniscus position, wherein said liquid zone comprises any remaining entities necessary for said operations or such additional entities are added to said liquid zone; and

detecting the interaction of said at least two entities in said liquid zone.

12. A method according to Claim 11, wherein said at least two entities comprise an enzyme, an enzyme substrate capable of producing a detectable product, and a compound being tested for its effect on the activity of said enzyme.

13. A method according to Claim 11, wherein said at least two entities comprise a ligand, a ligand receptor and a compound being tested for its effect on the binding of said ligand to said ligand receptor.

14. A method according to Claim 11, wherein said liquid zone is at least in part in a well through the wall of a capillary, said capillary channel is horizontal and connects two reservoirs with said well between said reservoirs.

15. A method according to Claim 11, wherein said compound is added to a reservoir in a non-aqueous solvent and is homogeneously distributed between said reservoirs and said capillary channel.

16. A method according to Claim 11, wherein said zone is at least in part in a well having a diameter of less than about 2mm and said capillary has a cross-sectional area of less than about one-half of said well

17. A method according to Claim 11, wherein said zone is less than about 500nl and adding comprises additions of less than about 300nl.

18. A method for performing a determination in a small volume, wherein said
5 determination comprises the interaction between at least two entities, said method comprising:

adding at least a portion of said at least two entities and optionally additional entities necessary for said determination to a liquid zone in a well comprising a liquid exposed to the atmosphere and subject to evaporation, said well being in liquid exchange relationship with a replenishing medium in a capillary channel, and said liquid in said well having a substantially
10 fixed meniscus position during said determination, wherein said liquid comprises any remaining entities necessary for said determination; and

detecting the interaction of said at least two entities in said liquid zone.

19. A method for performing a determination in a small volume, wherein said
15 determination comprises the interaction between at least two entities, said method comprising:

adding at least a portion of at least said two entities and any additional entities necessary for said determination to a liquid zone exposed to the atmosphere between the
20 termini of two capillary channels forming an unenclosed bridge, in contact with a replenishing liquid in said capillary channels, wherein liquid in said zone is subject to evaporation and said liquid zone comprises any remaining entities necessary for said operations;

incubating said volume for sufficient time for said interaction to occur; and

25 detecting the interaction of said at least two entities in said liquid zone.

20. A microfluidic device comprising:

a solid substrate comprising a plurality of microstructures comprising reservoirs, capillary channels and wells, each well connected to at least one reservoir by a capillary
30 channel, wherein said capillary channels and reservoirs are at least partially wettable, wherein said well has a cross-sectional area not greater than the cross-sectional area of said reservoirs and greater than the cross-sectional area of said capillary channel.

21. A device according to Claim 20, wherein said substrate is comprised of plastic.

22. A device according to Claim 20, wherein said device comprises a substrate having
5 said channels and reservoirs and a cover enclosing said channels and comprising said wells,
said cover comprising a wettable surface over said channels, said wettable microstructures
wetted by aqueous solutions.

23. A device according to Claim 20, further comprising an electrokinetic capillary channel
10 in fluid connection with said well.

24. A microfluidic device comprising:

a solid substrate comprising a plurality of microstructures comprising reservoirs,
capillary channels and wells, wherein at least a portion of said reservoirs are connected to a
15 common manifold, each of said wells is connected to a capillary channel linking said well to
at least one reservoir, wherein said capillary channels and reservoirs are at least partially
wetable, wherein said wells have cross-sectional areas not greater than the cross-sectional
areas of said reservoirs and not less than the cross-sectional area of said capillary channel

25. A microfluidic device according to Claim 24, wherein said channel is connected to
20 from 1 to 2 reservoirs of at least 1.2 times greater cross-section than said well.

26. A microfluidic device according to Claim 24, further comprising an electrophoretic
system comprising said well as part of said electrophoretic system, with a reservoir at a
25 terminus of a channel of said electrophoretic system for receiving an electrode.

27. A microfluidic device according to Claim 24, wherein said microfluidic device
comprises a central reservoir connected to a plurality of wells.

28. A microfluidic device comprising:

two opposed capillary channels with confronting orifices and an open space between said orifices, each channel connected to a reservoir; and means for moving liquid from the channels to the space between the channels.

29. A microfluidic device according to Claim 28, further comprising a platform between said capillary channels and in fluid communication with said capillary channels.

30. A microfluidic device according to Claim 28 having at least one row of a plurality of said two opposed channels, each channel connected to a reservoir; and means for moving liquid from each of said capillary channels to the space between said capillary channels, wherein said capillary channels are at least partially wettable, while said channels have cross-sectional areas not greater than the cross-sectional areas of said reservoirs.

31. A method for confining a solute within a small region of a liquid volume partially confined by a non-wettable border to form a meniscus, with said liquid volume in contact with said small region confined to a capillary channel, said method comprising:

adding said solute to said small region while liquid from said small region evaporates and liquid from said capillary flows into said small region to maintain said meniscus and said solute in said small region.

32. A method according to Claim 31, wherein said solute is added as a solution, wherein said meniscus equilibrates in relation to said non-wettable border after said adding.

33. A method for performing a determination where binding of a first entity to a second entity results in a change in a detectable signal, in a medium subject to evaporation under the conditions of said determination, said method comprising:

adding, in a volume of not more than about 300nl, a component for said determination to a liquid in a zone to form a reaction mixture of not more than about 500nl in liquid exchange with said liquid in a capillary channel, wherein other components necessary for said determination are added or contained in said liquid;

wherein evaporation occurs during said addition;

incubating said reaction mixture for sufficient time for binding to occur; and

detecting said detectable signal in said reaction mixture.

34. A method according to Claim 33, wherein said first and second entities are an enzyme and a candidate compound.

35. A method according to Claim 33, wherein said first and second entities are a protein and a candidate compound.

36. A microfluidic device comprising:

a solid substrate comprising a plurality of microstructures comprising reservoirs, capillary channels and wells, each well connected to at least one reservoir by a capillary channel, wherein said capillary channels and reservoirs are at least partially wettable, wherein said well has a cross-sectional area not greater than the cross-sectional area of said reservoirs and not less than the cross-sectional area of said capillary interface with said well and in liquid exchange relationship with said capillary, a side channel connecting said well to a capillary electrokinetic system comprising an analytical channel connected to said side channel and having reservoirs at its termini.

37. A microfluidic device comprising:

a solid substrate comprising a channel connecting two reservoirs having volumes of less than about 5 μ l and a cover plate enclosing said channel and having openings for said reservoirs and a well between said reservoirs in liquid connection to said channel; said well having a cross-sectional area not greater than said channel; and said cover having a hydrophilic surface above said channel.

38. A microfluidic device according to Claim 37, wherein said solid substrate is hydrophobic.